IT'S DIAGNOSIS, NOT DIAGNOSTICS
5th Innovation Academy:
It’s Diagnosis, Not Diagnostics

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   Save Babies Through Screening Foundation, UK

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16.00 Close
Welcome to our fifth Innovation Academy Scientific Symposium

Dr Dominic Harrington
MSc PhD

It gives me great pleasure to welcome you all to our fifth Innovation Academy Scientific Symposium, ‘It’s Diagnosis, Not Diagnostics’.

At our fourth symposium we explored how the delivery of ‘Next Generation Diagnostics’ is about more than a test or a therapy. It is about aligning multiple diagnostics, devices, IT and education platforms with the right expertise from an integrated network of skilled professionals, to deliver sustainable treatment pathways for better patient care in the future.

Today we build on that theme and will hear and learn about scientific innovations from 2015. Importantly we will also acknowledge that working at the limits of science in itself is not enough. We must also consider the wider healthcare community and constantly strive to improve the quality of the services we deliver to the patient.

Save Babies Through Screening Foundation, UK

Pat Roberts

Biography
Following a career in government working for the Department of Work and Pensions, Pat founded the charity Save Babies Through Screening Foundation (Save Babies UK) in 2008. Save Babies UK is a patient organisation, run entirely by volunteers and supporting families affected by a rare disorder, Krabbe Leukodystrophy.

The charity also advocates for the extension of the Newborn Screening programme in the UK for all appropriate inherited metabolic disorders. Pat is the Chair of the UK Patient Advocates for Newborn Screening Group, a member of the UK Lysosomal Storage Disorders Collaborative and a PPV member of the NHS England, Clinical Reference Group for Inherited Metabolic disorders. In her ‘spare’ time Pat sings and is a member of a UK and European Championship Barbershop Chorus.

Abstract
Scientific and medical advances ensure that diagnosis and our understanding of disease is becoming ever more sophisticated and reliable. However what does diagnosis really mean to families? How does it feel to be part of diagnostic uncertainty and to be on the receiving end of a diagnostic result? This presentation will explore the impact on families affected by rare disorders and why newborn screening extension is considered vitally important in achieving an earlier diagnosis.
Gary Nicholson trained in London in Microbiology before moving to Scotland to work in Dundee and Edinburgh. Now interim hub manager for Transforming Pathology Partnership at Ipswich, previously Gary was General Manager at Bedford for Viapath. Gary attended the “Future Leaders in Pathology” course run by the Department of Health and Royal College of Pathologists which led into the service improvement event and A3 thinking and has supported CQI for the Viapath Future Leaders in Innovation.
Do we know whether diagnostic medicine is achieving its purpose?

Andy Brogan

Biography
Andy has worked at senior management level in health and care organisations in England since 2004. Having cut his teeth as part of the team leading the integration of health and social care in Torbay, Andy now works at Vanguard Consulting, where he is practice lead for Health and Social Care. Andy’s work employs the Vanguard Method - a means to achieving exceptional levels of performance improvement through changing leadership thinking.

Abstract
Organisations worldwide are awash with examples of expensive change programmes which they have declared a success but where it appears that someone forgot to tell their customers. It is a consequence of the perspective taken. Seeing the world from the “inside-out” (i.e. from the organisation’s viewpoint and not the customers’) leads to a focus on the wrong measures and therefore the wrong problems. The “solutions” which result only serve to move rather than remove the real problems. The “solutions” which result only serve to move rather than remove the real problems, inflating costs.

Public services are no different. Whilst politicians and Whitehall crook about what their efficiency programmes have delivered, demand for public services continues to grow and budgets buckle. Rationalisations such as “an ageing population” or “rising expectations” are invoked to explain what’s happening but a weight of evidence suggests that their impact is far less than commonly assumed and that other factors are in play but outside of the accepted narrative.

A better way starts with adopting a different (“outside-in”) perspective. This means establishing a clear and constant purpose which is rooted in understanding how value is created with and for citizens. Taking this perspective promotes a fundamental shift in the thinking that governs how our public institutions are designed, managed and led and the resulting focus leads to real solutions to better problems. In the case of diagnostic medicine this means a move away from optimisation within the lab environment, replacing that with a deep understanding of the role of diagnostic medicine in supporting excellence in the health and care system at large.

Acting our way to a new way of thinking - changing the way we manage at Path Links

Dr David Clark

Biography
Consultant Cellular Pathologist - Path Links, Lincoln, UK Consultant Haematopathologist – Nottingham University Hospital, UK Honorary Senior Clinical Lecturer – Imperial College, London, UK

David undertook general professional training in general medicine and clinical haematology before training as a Histopathologist. He has a subspecialist interest in Haematopathology and is co-author (with Bridget Wilkins and Barbara Bain) of a textbook on bone marrow pathology and has contributed chapters to a number of other textbooks.

He was Clinical Director of Path Links (a managed pathology network across all five District General Hospitals in greater Lincolnshire) from its formation in 1998 until Feb 2014. He was a National Clinical Lead for Histopathology at NHS Improvement from 2011-2013. He is part of the team that developed and delivered 4 national CQI leadership programmes for senior Pathology professionals and Radiologists (2012-2014).

He currently works between Path Links and Nottingham University hospital where is part of the team developing an integrated Haematological Malignancy Diagnostic service for the East Midlands Cancer Network.

David is married with four grown up children and one grandchild, a dog and two cats.

Abstract
Lean is a comprehensive system of management based on the Toyota production system (TPS), encompassing all the activities of an organization. It focuses management activity on creating value for the end-user by continuously improving operational effectiveness and removing waste. Lean management creates a culture of continuous quality improvement with a strong emphasis on developing the problem solving capability of staff using the scientific method (Deming’s Plan, Do, Check, Act cycle).

Lean management systems have been adopted by a number of Histopathology departments throughout the world to simultaneously improve quality (reducing errors and shortening turnaround times) and lower costs (by increasing efficiency).

This article describes the key concepts that make up a Lean management system, and how these concepts have been adapted from manufacturing industry and applied to Histopathology using a case study of Lean implementation and evidence from the literature. It discusses the benefits, limitations and pitfalls encountered when implementing Lean management systems.

This paper was originally published in the Annual Review issue of Virchows Archiv 2015 as Quality improvement in basic histotechnology: the lean approach available as ‘Online First’ on http://link.springer.com/article/10.1007/s00428-015-1838-0
Putting purpose back into Pathology

Biography
Following a degree in Natural Sciences, Tom studied for a PhD in Dundee, followed by a post-doctorate in Bordeaux. Tom studied medicine in the West Midlands and has published on a variety of topics, from assessment of hospital cleaning to whole genome sequencing of MDR-Acinetobacter. Tom was appointed as Consultant Microbiologist in North Devon in 2010 and has been Lead Clinician for Pathology since 2012. Over the last few years, Tom has been particularly interested in how diagnostics can be used to redesign health systems.

Abstract
Tom will talk about how system conditions have led to laboratory medicine becoming increasingly divorced from what matters. He will discuss how a new approach to quality based on leading measures may help get us back on track.
Biography
Louise James is a Specialist Biomedical Scientist who works in the Metabolic Department at King’s College Hospital. Having recently achieved the IBMS Specialist Diploma in Biochemistry Louise is continuing to pursue her academic aspirations by undertaking an MSc in Blood Sciences. She is a member of the Future Leaders in Innovation Group, where she uses her leadership skills to promote innovation and expertise within Viapath. Her current interests include assisting in the development of further biogenic amine assays using LC-MS and the training of biomedical scientists and support staff alike.
HLA Typing by Next Generation Sequencing

Dr Robert Collins
BSc MSc PhD

Biography
Deputy Laboratory Director
Head of DNA & Stem Cell Transplantation
Clinical Transplantation Laboratory
Viapath at Guy’s Hospital.

Having completed a degree in Pharmacology in 1988, Bob worked at the Royal Veterinary College as a biochemical research technician, before moving to NHSBT-Tooting in 1991 to train as a state registered biomedical scientist. In 1993 Bob completed an MSc in Applied Haematology and began to specialise in white cell and platelet immunology.

Bob joined Guy’s and St. Thomas’ NHS Foundation Trust in 1996 working in the routine serology and DNA sections of the Clinical Transplantation Laboratory, supporting the South Thames renal transplant programme. Bob started a PhD in 1999 and in 2003 was state registered as a clinical scientist and became head of the advanced DNA section.

In 2006 Bob took responsibility for the work supporting stem cell transplantation and in 2007, having completed his PhD, he became deputy director of the laboratory. In 2009 Bob was seconded to Viapath and assumed the role of operations manager.

His special interests include stem cell transplantation, sequenced based HLA typing and MHC class I chain related genes.

Abstract
Introduction: Human leucocyte antigen (HLA) genes play an important role in the success of haematopoietic stem cell transplantation (HSCT), solid organ transplantation and are associated with autoimmune and infectious diseases. Current standards for HSCT and the high level of polymorphism make HLA genotyping by Sanger sequence-based typing (SBT) challenging. Ambiguous HLA typing results are often determined that require reflex testing to identify cis/trans nucleotides and, in some instances, define polymorphisms outside the region amplified. Next generation sequencing (NGS) techniques may resolve this issue through the combination of sequencing larger regions of genes and determining haplotype phase information using clonal amplification combined with software analysis. This study has evaluated NGSgo® (GenDx, Utrecht) using the MiSeq (Illumina, USA) platform against SeCore® (ThermoFisher Scientific, USA).

Methods: 48 Samples from external quality assurance (QA) schemes with known HLA types were selected for this study. DNA from each sample was amplified by PCR-SSP to generate individual amplicons for HLA-A,B,-C,-DRB1 and -DQB1 loci. Equimolar concentrations of each locus were pooled for each sample. Each pooled sample was fragmented, end-repaired, dA-tailed and cleaned up using magnetic beads to size select DNA fragments of ~600 bp. Each end of the DNA fragments was labelled with unique indices for paired-end sequencing. DNA clean up and size selection was repeated and the samples pooled. A pre-determined concentration was loaded into a MiSeq nano-cell for sequencing. The raw data was submitted to NGSEngine® for analysis against the IMGT/HLA database (version 3.20, April 2015) to determine the HLA types.

Results: 203 loci were analysed from 41 samples and 198 (97.5%) were concordant with the HLA types obtained previously. Two HLA-DRB1 loci failed to amplify for subsequent analysis. Four of the five loci with discrepant results were HLA-DRB1 and two of these contained nucleotide mismatches with the IMGT/HLA database. One HLA-A type differed from the original with a null allele being identified. The results submitted to the QA schemes as determined by SBT contained 26.1% ambiguities, whereas the results from NGSgo® contained 1.5% ambiguities.

Conclusion: Other studies have shown up to 99% concordance between HLA typing by various NGS methods and SBT, so 97.5% concordance suggests a high quality product following comprehensive development by the manufacturer. The failure of two amplifications (~1%) is consistent with the level seen in our laboratory for other PCR-SSP methods. The HLA-DRB1 locus discrepancies could not be resolved and suggest optimisation is required, but the HLA-A locus discrepancy was correct. HLA typing by NGSgo® is a comparable method to SeCore® SBT, but can resolve a higher percentage of ambiguities without additional work. NGSgo® is not suitable for low throughput due to MiSeq reagent costs. There is a minimum number of samples that must be batched to be comparable with the costs associated SeCore® SBT, but it is scalable and a low cost method providing high resolution HLA typing when used at high throughput.
Cytokine array analysis in haematological disorders and in alcoholism

Biography
Gemma has been working at King’s College Hospital since 2010, initially as a regionally funded Trainee Clinical Scientist, completing an MSc in Clinical Biochemistry in 2012. She holds a BSc in Biochemistry from the University of Bath. Since gaining registration as a Clinical Scientist with the Health and Care Professions Council, she has been working in the busy Contract Research team at Viapath where she has developed an interest in measuring cytokines.

Abstract
The important role of cytokines and chemokines in both pro-inflammatory and anti-inflammatory states has been well known for many years. This has led to several conditions being identified that are caused by excess production and release of cytokines. Castleman’s disease (CD) is a rare non-malignant inflammatory condition with diverse symptoms and high morbidity and mortality rates that is associated with marked increases in interleukin-6 (IL-6). About 30% of patients with CD are associated with POEMS syndrome with evidence of a paraprotein, peripheral neuropathy and osteosclerosis. POEMS syndrome is linked to excess Vascular Endothelial Growth Factor (VEGF). The pharmaceutical industry has developed humanised antibodies against the receptor to IL-6 (tocilizumab) and IL-6 itself (siltuximab). It is proposed that measuring cytokines in plasma may aid in guiding treatment and monitoring disease activity.
Identification and diagnosis of epidermolysis bullosa simplex skin disease with exophilin-5 defects using immuno-histochemistry and modern electron microscopic methods

Biography
The National Diagnostic Epidermolysis Bullosa (EB) Laboratory at St Thomas’ St. John’s Institute of Dermatology Viapath LLP at St Thomas’ Hospital.

James McMillan started his scientific career after graduating from the University of York (studying Human & Applied Biology) and the University of London (studying Master of Science in Experimental Pathology and Toxicology). In 1990 he joined the Department of Cell Pathology and his scientific career progressed as a research associate while he gained a Ph.D. (from King’s College, London) examining human skin development and the group of blistering skin diseases that comprise epidermolysis bullosa (EB) and related congenital skin disorders.

He later became a Welcome-funded Postdoctoral Research Fellow, studying the role of the keratin intermediate filament associated proteins including plectin in skin and muscle disease and identified the first human genodermatosis affecting desmosomal keratinocyte junctions with mutations in the gene encoding plakophilin-1 leading to skin fragility and hair loss.

Between February 2000 and 2004 Dr. McMillan completed further postdoctoral training, working on skin and muscle at Hokkaido University Graduate School of Medicine, Dermatology in Sapporo, Japan. In 2004, Dr. McMillan became Professor of skin tissue engineering within the Faculty of Science at Hokkaido University, Japan devising new skin grafting treatments.

In 2008 Dr McMillan became Head of the Burns Research Laboratory at the Royal Children’s Hospital in Brisbane, Queensland where he studied skin burn tissue engineering and skin cell cytokine expression. In 2012 James returned to the UK to join the National Diagnostic Epidermolysis Bullosa Laboratory as the Clinical Scientist lead in microscopy.

Dr. McMillan has an impact factor of over 400 and has published over 85 original articles in peer-reviewed journals including Nature Genetics, Genes and Development and more recently Nature Medicine. His greatest achievement has been in identification of the underlying causes of different genetic skin diseases affecting important structural skin proteins.

Abstract
Microscopy Lead, National Diagnostic Epidermolysis Bullosa (EB) Laboratory Viapath LLP, St John’s Institute of Dermatology, St Thomas’ Hospital, London, UK.

Epidermolysis bullosa (EB) comprises a group of genetic skin diseases classified into three major subtypes depending on the level of skin cleavage within the epidermal keratinocyte or basement membrane zone and is caused by defects in one of approximately 18 distinct genes. Tissue separation occurs either within the basal keratinocyte epidermal cytoplasm, through the lamina lucida, or in sub-lamina densa region of the dermal epidermal junction in EB simplex, junctional EB, and dystrophic EB, respectively. Indirect immunofluorescence (IF) antigen mapping and transmission electron microscopy (TEM) have proved effective to determine the level of tissue separation and hemidesmosome (HD)-anchoring filament/fibril component defects if performed by experienced operators. IF and TEM have also proven to be a powerful techniques for the diagnosis of new subtypes of EB with novel genetic defects. Recent advances in EB next generation screening combined with better microscopic tests such as 3View EM will enable us to improve the diagnostic efficiency of EB simplex cases with defects in exophilin-5 (EXPH5).

Our overall aim is to improve our understanding of the pathogenesis of all rare and difficult-to-diagnose EB subtypes particularly those involved in unexpected epidermal keratinocyte functions.
Biography
Principal Clinical Scientist, Inherited Metabolic Disease Laboratory. Michaela came to Viapath in 2009 as a trainee on the NHS London Clinical Scientist training program. Guy’s and St Thomas’ served as her host institution. After completing her training period and spending time in various laboratories, she was fortunate to obtain a permanent position within the IMD laboratory. She completed the London MSc in Clinical Biochemistry with Distinction in 2011 and achieved FRCPath Part 1 in March 2013. She is a registered Clinical Scientist with the Health and Care Professions Council.

Michaela is a member of the British Inherited Metabolic Diseases Group (BIMDG), which is the National group for professionals working in the field of IMD and also serves on the BIMDG committee where she is the representative for scientist trainees and Editor of the BIMDG Bulletin, the official newsletter of the group.

Abstract
Development of a stable isotope tandem mass spectrometry method for the measurement of homogentisic acid in patients with Alkaptonuria.

It is caused by lack of the enzyme homogentisic acid dioxygenase which results in the accumulation of homogentisic acid (HGA) in cartilage, connective tissue, plasma and urine of affected patients. AKU typically presents in the 3rd or 4th decade of life with severe premature arthritis, pigmentation (also called ochronosis) leading to multiple joint replacements and ultimately a wheelchair-bound existence. Until recently treatment options were limited to analgesia and symptomatic measures, with dietary manipulation and vitamin C being of limited value. However, Nitisinone, a potent inhibitor of the second enzyme in the tyrosine catabolic pathway has recently been suggested as potential therapy. A three-year follow-up study was encouraging, with significant reduction (up to 95%) of urinary HGA following Nitisinone treatment.

The aim of this project was to develop and validate a robust stable isotope mass spectrometry assay to quantify urinary HGA in patients with Alkaptonuria with a view to monitoring response to treatment. A method for urinary HGA was developed and validated using LC-MS/MS with negative electrospray ionisation. A study was undertaken to compare samples from patients with Alkaptonuria in conjunction with the Mayo Clinic. This method is useful in confirming the presence of HGA as a diagnostic marker for Alkaptonuria and also for monitoring known patients undergoing treatment.
Next generation sequencing as first line screening for the diagnosis of inherited metabolic diseases

Biography
Dr Tony Marinaki is a Consultant Clinical Biochemist in Biochemical Sciences at St Thomas’ Hospital. Tony joined the Purine Research Laboratory in 1999. His current research focuses on improving the diagnosis of inherited metabolic diseases and the pharmacogenetics of purine and pyrimidine drug analogues.

Abstract
The diagnosis of inherited metabolic disorders (IMD) is clinician-led, with the evolving clinical presentation directing laboratory testing beyond the standard acute metabolite screens. Nationally, there are specialist services for most metabolic disorders, however no single UK laboratory is able to offer tests for the diagnosis of all metabolic disorders. As a result, just one-third of inherited metabolic defects are diagnosed by the age of one year.

Limited clinical exome sequencing should be considered as a first line screening test able to diagnosis most genetic disorders in a single assay. However, there are concerns that the number of false positives may be high, leading to unnecessary and costly investigations.

In collaboration with the Metabolic Consultants at the Evelina London Children’s Hospital, we undertook a proof of concept study to demonstrate that limited clinical exome sequencing has potential as a first line IMD screening test. We were blinded to all patient clinical and demographic information. Although at the time of writing, we are still blinded to the true metabolic defect in these patients, we are confident that in two thirds of patients we have made the correct diagnosis. The next step is to trial limited clinical exome sequencing in the clinic to demonstrate benefit to patients and their families, and provide evidence of cost savings to the NHS.
Following the success of last year’s Richard Hurst Memorial Prize, the Viapath Excellence in Pathology Award 2015 celebrates cutting-edge scientific work being performed by staff across all of our sites.

Abstracts of up to 250 words were submitted to an expert panel of judges from within our organisation, and the three finalists have been invited today to present their work as 5 minute lightning talks. The Viapath Excellence in Pathology Award 2015 will go to the best talk on the day as voted by the audience.

Rob Dunn
Clinical Scientist in Cancer Genetics, Guy’s Hospital

With thanks to the 2015 Judges:

Dr RS Carling
Consultant Clinical Scientist and Director of Biochemical Sciences, St. Thomas’ Hospital

Professor RA Sherwood
Consultant Clinical Scientist and Viapath Scientific Director, King’s College Hospital

Dr M Smith
Principal Clinical Scientist in Infectious Diseases, King’s College Hospital

Dr WS Wassif
Consultant in Clinical Biochemistry and Metabolic Medicine, Bedford Hospital

Dr B Wilkins
Consultant Histopathologist, St. Thomas’ Hospital
Measurement of vitamin K metabolites in neonatal stool samples allows non-invasive comparison of vitamin K metabolism in term and pre-term neonates

Abstract
Nutristasis Unit, Viapath, St. Thomas’ Hospital, London, UK

Prophylactic phytomenadione (vitamin K1) effectively prevents vitamin K deficiency bleeding of the newborn. However there are currently insufficient data to inform further dose optimisation which may be desirable, particularly for preterm infants.

Comparison of vitamin K metabolite excretion indicated preterm neonates have a reduced rate of vitamin K metabolism during the first 12 weeks of life, which reaches rates equivalent to term neonates between 5 and 12 weeks of life. There was no significant difference in the relative abundance of the two metabolites in the two groups (preterm mean 7C excretion = 35.2 % of total metabolite excretion, term = 36.0%). Mean faecal vitamin K metabolite excretion was markedly elevated in formula vs. breast milk fed neonates.

The assessment of vitamin K status by measurement of vitamin K metabolite excretion in stool samples may allow a non-invasive means to refine phytomenadione dosages in neonates.
EvE: In silico hybridisation of embryos for microarray studies in Pre-implantation Genetic Diagnosis

Aled Jones

Biography
Aled is in his final year of the NHS Scientist Training Program in Clinical Bioinformatics based within the Viapath Genetics Laboratories. Before moving to London he spent four years in the Cytogenetics department of St Mary’s Hospital, Manchester and before that a year in a forensics company near Oxford. In between Oxford and Manchester he undertook an MSc in Medical Genetics at Newcastle University. Outside of work he enjoys rugby, running, curries, travelling and gadgets.

Abstract
Array CGH is used for pre-implantation genetic diagnosis (PGD) of embryos with abnormal copy number variation. DNA from an embryo and a reference sample is labelled with fluorescent dyes before being hybridised to an array containing 60,000 oligonucleotide probes. At each probe the signal intensity of each dye is measured, normalised and the log(2) ratio between samples calculated. The log(2) ratios are used by an algorithm to call regions with abnormal copy number variation.

A more efficient method would be to hybridise one embryo to another embryo; however, due to the risk of one embryo failing and therefore making the other embryo unanalyisable, this is not current practice.

Embryo vs Embryo (EvE) is an algorithm which allows hybridisation partners to be analysed independently. Any two samples can be re-hybridised in silico, using signal intensities to calculate a new log(2) ratio which can be analysed as if they were hybridised in vitro.

Preliminary results show samples re-paired by EvE are concordant with the expected result. EvE allows embryo to embryo hybridisation with no danger of a failing embryo affecting the hybridisation partner, halving consumable costs and processing time.

In addition, samples of different material (eg embryo and reference DNA from cultured cells) are labelled with varying efficiency, affecting the signal intensities and therefore the log(2) ratios and calling algorithm. Hybridising embryo to embryo reduces this variation increasing the test sensitivity and specificity.
Generation of reference intervals for two automated, new-generation von Willebrand factor activity assays on a large donor population

Biography
Kazia is a biomedical scientists registered since December 2012. She has been employed by Viapath since May 2009. She is now a specialist BMS since passing her specialist exam two weeks ago. She is still involved in the ongoing von Willebrand collaboration project with scientists from Belgium.

Abstract
Background: Circulating von Willebrand factor (VWF) levels are influenced by a variety of biological factors. Normal individuals with O blood group demonstrate 25% -35% lower VWF levels than non-O individuals.

Aims: To generate general and blood group-specific reference intervals (RIs) for 2 new-generation VWF activity assays on a large donor population.

Methods: The HemosIL VWF:RCo assay (on an ACL TOP 500) involves binding plasma VWF to recombinant GpIbα fragments attached to latex particles with the aid of ristocetin. The Innovance VWF:GpIbM assay (on a Sysmex CS2000i) utilises a recombinant GpIbα containing two gain-of-function mutations and is ristocetin-independent. VWF antigen (VWF:Ag) was determined using HemosIL VWF:Ag immunoassay on the ACL TOP 500.

Results: Three parameters were derived from each of the 201 plasma samples obtained from healthy donors. 183/201 samples had a known ABO blood group. RIs were calculated as 95% confidence limits. Median (M) and RI values are presented as follows: Non-O blood group (N=84): VWF:Ag: 110.8; 64.5-185.5; VWF:RCo: 97.7; 50.1-153.5; VWF:GpIbM: 100.1; 37.1-164.3. Group O (N=95): VWF:Ag: 82.8; 53.2-127.4; VWF:RCo: 72.3; 44.8-123; VWF:GpIbM: 66.8; 31.6-105.1.

Combined results, irrespective of blood group, (N=201): VWF:Ag: 94.2; 53.3-169.7; VWF:RCo: 86.6; 47.0-152.9; VWF:GpIbM: 80.2; 38.0-165.2. All results are expressed in IU/dL.

Conclusion: Blood group significantly influences VWF levels and it is important to use blood group specific reference intervals for the diagnosis of VWD. The VWF activity values also depend on the method of analysis applied. VWF:GpIbM demonstrates lower values for VWF activity when compared with VWF:RCo. Reagent / analyzer specific RIs should be locally determined.
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Biography
Professor Roy Sherwood is Consultant Clinical Scientist and Scientific Director of Viapath at King’s College Hospital. He trained at the Royal Sussex County Hospital, Brighton. In 2013 he became Professor of Clinical Biochemistry at King’s College London. He has an interest in biomarkers in liver, gastrointestinal and cardiovascular disease in particular.

He has built up an interest in tumour markers associated with endocrinology and neuroendocrine tumours and the laboratory at King’s will soon be offering a comprehensive service for these. He has a BSc in Clinical Biochemistry from Salford University and MSc in Clinical Biochemistry from Surrey University and a DPhil from Sussex University.
Is there a need for monitoring NOAC levels in routine practice?

Biography
Dr Jignesh Patel holds a clinical academic position, specialising in anticoagulant drug therapy and is based between the department of haematological medicine, King’s College Hospital and the Institute of Pharmaceutical Science, King’s College London.

Following qualification as a pharmacist, Jig has worked as a clinical pharmacist in a number of hospitals across London and the South East. Jig was awarded a NIHR Guy’s and St. Thomas’ / King’s College London BRC allied healthcare professional research training fellowship in 2009. Jig’s thesis focussed on the pharmacokinetic changes of enoxaparin during the antenatal period, in order to determine the optimal dosing strategy of enoxaparin for the treatment of antenatal venous thromboembolism. This research saw collaboration between the laboratories of Prof Roopen Arya (King’s College Hospital, UK), Prof Graham Davies (King’s College London, UK) and Dr Bruce Green (Model Answers Pty Ltd, Australia).

Jig’s research is concerned with the optimal use of anticoagulant therapy in clinical practice and primarily focuses on addressing anticoagulant drug dosing issues where uncertainties exist. This work involves pharmacokinetic modelling of the anticoagulants, including the direct oral anticoagulants.

In addition, Jig is responsible for directing the King’s Anticoagulation Reference Centre: http://www.kingsthrombosiscentre.org.uk/index.php/anticoagulation

Abstract
Oral anticoagulation therapy is prescribed for millions of patients worldwide for the prevention and treatment of arterial and venous thrombosis. With the arrival of a number of direct oral anticoagulants (DOACs), the anticoagulation landscape is changing. These agents offer many advantages over the vitamin K antagonists: rapid onset of action, less propensity for drug-drug and drug-food interactions and predictable pharmacokinetic profiles. In the UK, the availability of DOACs in clinical practice is currently driving change in the delivery of anticoagulation services. The licensing authorities and the manufacturers of these agents suggest that routine monitoring of anticoagulant effect is not required. Furthermore, long-term follow-up of patients prescribed DOACs is not required. However, anticoagulants can be considered as drugs with a narrow therapeutic index. Therefore, the lack of monitoring and formal follow-up with DOAC therapy, could lead to problems.

At King’s, we began prescribing DOACs for our patients, according to guidance issued by the South London stroke and cardiac network in August 2012. Although our early experience in a real-world population has largely been positive, a number of uncertainties have arisen with their use. The talk will explore some of these uncertainties and what role, if any, there is with the laboratory monitoring these agents.
Measuring systemic markers of inflammation as a novel link between depression and type 2 diabetes

Biography
Calum Moulton is a Specialist Registrar in Psychiatry and NIHR BRC Preparatory Clinical Fellow in the Diabetes and Psychiatry Group of the Institute of Psychiatry, Psychology and Neuroscience, King’s College London, led by Professor Khalida Ismail. He previously worked as an Honorary Visiting Clinical Fellow in the Department of Infection, Immunity and Inflammation, University of Leicester, before joining the Diabetes and Psychiatry Group as an Academic Clinical Fellow in 2012. His main interests are in the mechanisms underlying the links between type 2 diabetes and both depression and cognitive impairment, in particular the role of innate immunity and inflammation. He is first-author of the recent review, ‘The link between depression and diabetes: the search for shared mechanisms’, published in The Lancet Diabetes and Endocrinology.

He has presented findings from the South London Diabetes Study at both the European Association for the Study of Diabetes and Diabetes UK. His first-author publications have examined the relationships between type 2 diabetes and depression, cognitive function and grey matter effects. Calum also has a strong interest in music, authoring the recent review ‘Perfect Pitch Reconsidered’ that was published in Clinical Medicine, and he was recently awarded the Licentiate of the Royal Schools of Music in viola performance.

Abstract
Depression affects up to 20% of people with type 2 diabetes and predicts increased risk of diabetes complications, dementia and premature mortality. Yet the reasons for this are poorly understood and poorly explained by lifestyle factors. Elevated inflammation has been strongly implicated in the pathogenesis of depression and type 2 diabetes, respectively, but until recently no research had examined inflammation as a common link between the two conditions. In the South London Diabetes (SOUL-D) study, a unique multi-ethnic cohort of 1790 people with new-onset type 2 diabetes, we measured a panel of 12 markers of innate immunity and inflammation. Despite no difference in glycaemic control, concentrations of C-reactive protein (CRP), interleukin-1, IL-1-receptor antagonist, monocyte chemotactic protein-1, white blood cell count, and triglycerides were associated with increased depressive symptoms, even after adjustment for potential confounders.

Furthermore, differences in CRP concentrations between depressed and non-depressed patients persisted after 1- and 2-year follow-up, suggesting a persistent effect of inflammation on depressive symptoms. Finally, in patients prescribed incretin-based therapies (which have potent anti-inflammatory properties), there was significant improvement in mood from baseline to 1-year follow-up, which correlated with reduction in CRP but not with change in glycaemic control. Collectively, this suggests that elevated inflammation is involved in the pathogenesis of depressive symptoms in type 2 diabetes.

Moreover, elevated inflammation may provide a novel target to treat depression and diabetes simultaneously, thereby improving morbidity and mortality in this high-risk group.
Bile acids cause liver disease and a whole lot more

Biography
Richard Thompson studies cholestasis and bile flow. He does this mainly through genetic analysis. This has led to the discovery of several new diseases and the identification of normal physiological processes. He is the Professor of Molecular Hepatology, and divisional Postgraduate Tutor within KCL. He is an Honorary Consultant Paediatric Hepatologist, Clinical Lead for the 100k Genome Project, and Clinical Lead for Liver Molecular Genetics with KCH.

Abstract
In the course of evolution we have acquired the ability to synthesise highly detergent bile acids. This probably occurred out of a need to extract efficiently lipids from our diet. This has several consequences.

We are now more efficient at extracting fat from our diet than would be ideal given the nutrition available to us. These bile acids have become important signalling molecules; probably for the reason of their toxicity, but also due to their central role in lipid metabolism.

Defects in several aspects of bile acid handling and regulation have become evident through the study of cholestatic liver disease. Gestation compared to case controls (P<0.001). Our results raise the possibility of an alternative test to an oral glucose tolerance test for the diagnosis of gestational diabetes.
We would like to extend our sincere thanks to all the speakers at this fifth Innovation Academy symposium and to other members of the wider team who have made this event possible.

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